

both aortic NE (median:318 to 337 pg/ml) and CS NE (median 368 to 542 pg/ml) in all pts and doubled the transcardiac spillover of NE (median -99 to -198 pg/ml<sup>A</sup>) whereas aortic, CS and transcardiac NE were not significantly modified during P (median spillover -88 to -128 pg/ml; NS) or DOF (median spillover -82 to -69 pg/ml; NS) infusions. Thus, in contrast to DOF, IV AMIO significantly increased cardiac sympathetic drive which could partially explain the smaller QT prolongation and the low incidence of torsades de pointes during IV AMIO administration. Further studies are needed to determine if this phenomenon could also limit the acute antiarrhythmic activity of IV amiodarone. \*  $p < 0.05$  vs P; <sup>A</sup>  $p < 0.05$  vs DOF

### 1015-37 Early Efficacy and Complications of Initiating Amiodarone for Atrial Fibrillation in Advanced Heart Failure

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**Background:** The effects of initiating amiodarone (AM) are not well-defined for pts with atrial fibrillation (AFib) and advanced heart failure (HF).

**Methods:** Records were reviewed for 37 consecutive pts undergoing AM initiation for AFib after HF service admission. Rhythm at last follow-up was determined for all pts. HF was due to CAD (16.43%) alcohol (3.8%), valve disease (3.8%) or idiopathic (15.40%). Age was  $60 \pm 10$  yrs, NYHA class  $3 \pm 1$ , LVEF  $24 \pm 7\%$ , LA dimension  $5.3 \pm 0.8$  cm, median AFib duration 12 mos. Pts received oral AM starting at  $1.2 \pm 0.2$  gm/day.

**Results:** AM was decreased to  $<600$  mg/day in 9 pts (24%), due to bradycardia in 5 (14%), worsening HF in 2 (5%), and GI upset in 2 (5%). Bradycardia led to permanent pacemaker in 7 pts and stopping digoxin in another 8 pts. Conversion to sinus rhythm occurred spontaneously in 3 pts and with electrical cardioversion in 26 (after  $7 \pm 2$  gms total AM), for 78% initial success. After median follow-up 9.5 mos, 21 (57%) of all pts were still out of AFib. After discharge, 3 pts had hypothyroidism, another had hypothyroidism and abnormal liver function, and 1 showed neurotoxicity.

**Conclusion:** AM with electrical cardioversion has high initial and moderate later success for AFib and advanced HF. The major early morbidity is bradycardia, requiring pacemaker or discontinuation of digoxin in 41% of pts.

### 1015-38 Which Patients With Left Ventricular Dysfunction Require Chronic Anticoagulation? A Prospective Analysis

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**Background:** The current AHCPR guidelines for CHF disease management do not recommend the routine use of chronic anticoagulation and cite the lack of randomized trials in this area. However, warfarin is used routinely by many practitioners with the goal of prevention of LV thrombus formation and subsequent embolization. We set out to investigate the risk profile of those patients with LV thrombus identified by echocardiography as part of a heart transplantation evaluation.

**Methods:** We identified 28 cases with LV thrombus in a 144 patient consecutive series with longitudinal follow-up for a median of 25 months. Patients with prosthetic valves or EF  $>35\%$  were excluded. Using an unmatched case-control design and multivariate techniques, 35 clinical and echocardiographic variables were evaluated for their independent relationship to LV thrombus formation and subsequent thromboembolism.

**Results:** The mean age of cases ( $n = 28$ ) and controls ( $n = 116$ ) was  $50.2 \pm 11.0$  vs.  $54.2 \pm 11.1$  years, with 22 (78.6%) and 78 (67.2%) being male,  $p > 0.05$ . The mean EF was  $17.5 \pm 5.5$  vs.  $20.0 \pm 6.9$  respectively,  $p > 0.05$ . The groups were likewise similar with respect to baseline characteristics, medication use, and comorbidities. Multiple logistic regression revealed an ischemic etiology of the cardiomyopathy, OR = 3.04, 95% CI 1.04-8.83,  $p = 0.04$  and LV chamber size (LVDD mm unit increment above referent), OR = 1.09, 95% CI 1.03-1.16,  $p = 0.004$ , to be independent predictors of LV thrombus formation when controlling for warfarin and ASA utilization. All thrombi appeared at LVDD  $>60$  mm with a consistent, graded relationship seen between thrombi frequency and increasing chamber size. Peripheral embolism occurred in 5 (17.9%) vs. 13 (11.2%) of cases and controls respectively,  $p = 0.34$ .

**Conclusions:** These data support a risk-adjusted approach for the decision to use warfarin in CHF patients. Those patients with ischemic cardiomyopathies and dilated LV chamber sizes (LVDD  $>60$  mm) appear to be at particularly high risk. Future randomized trials in this group are warranted.

### 1015-39 Dofetilide, a New Class III Antiarrhythmic Drug Reduces Hospital Admissions for Congestive Heart Failure - Secondary Endpoints of the DIAMOND-CHF Study

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**Background:** The DIAMOND-CHF study demonstrated that dofetilide was safe in patients with congestive heart failure (CHF). One of 8 secondary endpoints was hospital admissions for worsening of congestive heart failure.

**Methods:** In the DIAMOND study 1518 patients admitted to hospital with CHF and with severe left ventricular systolic dysfunction (wall motion index  $\leq 1.2$ , corresponding to ejection fraction below 35%) were randomised to receive dofetilide (0.25-1 mg daily) or placebo in a double blind study. Minimal follow up was 12 months. Eight secondary endpoints were: Hospital admission with CHF requiring increase in treatment of CHF, subtypes of death (cardiac, arrhythmic, cardiac + cardiac arrest), arrhythmias requiring treatment, cardiovascular events in patients with atrial fibrillation, myocardial infarction, death after dosing change of dofetilide (after 300 patients).

**Results:** There were 228 hospital admission with worsening of CHF on dofetilide and 290 on placebo. The risk reduction was 0.75 with 95% confidence limits 0.63-0.89,  $p < 0.001$ . This risk reduction was seen in patients with AF as well as those who maintained sinus rhythm. All other secondary endpoints were neutral.

**Conclusion:** Dofetilide has a marked effect on hospital admissions for worsening of CHF. This effect appears to be partially independent of the effect of the drug on atrial fibrillation.

### 1015-40 Angiotensin II Receptor Antagonist Improves the Immune Activations of Patients With Chronic Heart Failure

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**Background:** Not only neurohumoral but also immune activation may have an important role in the progression of congestive heart failure (CHF). Chronic effects of angiotensin II (ang II) type 1 receptor antagonist on the immune system remains unknown.

**Methods:** To determine the chronic effects (14 weeks) of ang II type I receptor antagonist (TCV-116) on plasma levels of cytokines and soluble adhesion molecules were evaluated in mild to moderate CHF patients ( $n = 14$ , ejection fraction (EF)  $<45\%$ , NYHA class II-III) and compared with placebo ( $n = 8$ ).

**Results:**

	NYHA class	EF %	Ang II pg/ml	IL-6 pg/ml	TNF- $\alpha$ pg/ml	sICAM-1 ng/ml	sVCAM-1 ng/ml
Pre-TCV	2.5	37	34	4.8	5.4	324	865
TCV	1.8*	41*	60*	2.5*	4.3*	269*	669*

(IL-6 = interleukin 6, TNF- $\alpha$  = tumor necrosis factor  $\alpha$ , sICAM-1 = soluble intercellular adhesion molecule-1, sVCAM-1 = soluble vascular adhesion molecule-1 \*  $p < 0.05$  vs. pre-TCV).

There was no significant changes of clinical parameters and neurohumoral and cytokines levels in the placebo group. In contrast, plasma levels of IL-6, TNF- $\alpha$ , sICAM-1, and sVCAM-1 were significantly decreased coincident with the increase in EF and with improvements in symptoms in the TCV group.

**Conclusion:** These findings suggest that the chronic treatment of ang II type 1 receptor antagonist improve the activations of the immune system in patients with CHF.